43. A method for inhibiting a humoral immune response comprising contacting T-cells with an antibody that binds specifically to CD40CR.

44. A method for inhibiting immunoglobulin production comprising contacting T-cells with an antibody that specifically binds to a protein specifically recognized by monoclonal antibody MR1 produced by the hybridoma having ATCC Accession No. HB 11048.

45. A method for inhibiting immunoglobulin production comprising contacting T-cells with an antibody that specifically binds to CD40CR.

46. A method for inhibiting activation of B-cells comprising contacting T-cells with an antibody that specifically binds to a protein specifically recognized by monoclonal antibody MR1 produced by the hybridoma having ATCC Accession No. HB 11048.

47. A method for inhibiting activation of B-cells comprising contacting T-cells with an antibody that specifically binds to CD40CR.

48. A method for inhibiting a humoral immune response in an animal comprising the step of administering to the animal in an amount effective to inhibit the humoral immune response, an antibody or fragment thereof that binds specifically to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 11048.

49. A method for inhibiting a humoral immune response in an animal comprising the step of administering to the animal, in an amount effective to inhibit the humoral immune response, an antibody or fragment thereof that specifically recognizes CD40CR.

50. A method for inhibiting immunoglobulin production in an animal comprising the step of administering to the animal, in an amount effective to inhibit immunoglobulin production, an antibody or fragment there of that specifically binds to a protein specifically recognized by the hybridoma having ATCC Accession No. HB 11048.

51. A method for inhibiting immunoglobulin production in an animal comprising the step of administering to the animal, in an amount effective to inhibit

immunoglobulin production, an antibody or fragment thereof that specifically recognizes CD40CR.

52. A method for inhibiting activation of B-cells in an animal comprising administering to the animal, in an amount effective to inhibit activation of B-cells, an antibody or fragment thereof that specifically binds to a protein specifically recognized by monoclonal antibody MR1 produced by the hybridoma having ATCC Accession No. HB 11048.

53. A method for inhibiting activation of B-cells in an animal comprising administering to the animal, in an amount effective to inhibit activation of B-cells, an antibody or fragment thereof that specifically recognizes CD40CR.

54. The method of any one of Claims 42 through 53, wherein the antibody or fragment thereof is selected from the group consisting of monoclonal antibodies, chimeric antibodies, human antibodies, and fragments thereof.

55. The method of any of Claims 42 through 53, wherein the antibody or fragment thereof is conjugated to another moiety selected from the group consisting of an enzyme, toxin, growth factor, lymphokine, anti-proliferative agent, alkylating agent,

anti-metabolite, antibiotic, vinca alkaloid, platinum coordinated complex, radioisotope, and fluorescent compound.

56. The method of any one of Claims 42 through 53, wherein the antibody is conjugated to a therapeutic agent.

57. The method of any of Claims 48 through 53, wherein the animal is a mammal.

58. The method of any of Claims 48 through 53, wherein the animal is a human.

REMARKS

By the present amendments, new claims have been presented in favor of the original claims (which are cancelled), all of which correspond to the same invention claimed in Lederman et al, 5,993,816, issued on November 30, 1999. Specifically,

Claims 42 and 43 correspond to Claim 1 of Lederman '816;

Claims 44 and 45 correspond to Claim 2 of Lederman '816;

Claims 46 and 47 correspond to Claim 3 of Lederman '816;

Claims 48 and 49 correspond to Claim 4 of Lederman '816;

Claims 50 and 51 correspond to Claim 4 of Lederman '816;

Claims 52 and 53 correspond to Claim 5 of Lederman '816;

Claim 54 corresponds to Claim 7 of Lederman '816;

Claims 55 and 56 correspond to Claims 9 and 10 of Lederman '816;

Claim 57 corresponds to Claim 13 of Lederman '816; and

Claim 58 corresponds to Claim 14 of Lederman '816.

Specific support for the newly-submitted claims may be found in the as-filed application as follows:

Claims 42, 43: Section 5.4 at pages 17-19, original Claims 22, 24, 27, 28, 29, 30, 31, 32, 37; Section 6.24 at pages 28-31, et seq.

Claims 44, 45: Section 5.4 at pages 17-19, original Claims 22, 24, 27, 28, 29, 30, 31, 32, 37; Section 6.24 at pages 28-31;

Claims 46, 47: Section 5.4 at pages 17-19, original Claims 22, 24, 27, 28, 29, 32, 37; Section 6.24 at pages 28-31;

Claims 48, 49: Section 5.4 at pages 17-19, original Claims 22, 24, 27-32, 37; Section 6.24 at pages 28-31;

Claims 50, 51: Section 5.4 at pages 17-19, original Claims 22, 24, 27-32, 37; Section 6.24 at pages 28-31;

Claims 52, 53: Section 5.4 at pages 17-19, original Claims 22, 24, 27-32, 37; Section 6.24 at pages 28-31;

Claim 54: the specification at page 12, lines 1 to page 13, line 21, et seq.;

Claim 55: the specification at page 11, lines 29-35, et seq.

Claim 56: the specification at page 11, lines 29 to 35, et seq.

Claims 57, 58: original Claims 30-32, 37, 38, 39, and Section 6.24 of the specification (*et seq.)*.

Thus, it can be seen that all of the newly-submitted claims are directed to methods of using antibodies specific to CD40L (also known in the art as CD40CR, gp39, CD154, 5c8 antigen, TBAM) to inhibit humoral immunity, immunoglobulin production and B-cell activation. Such inhibition results because this antibody binds CD40L, which is an antigen expressed on activated T-cells that is involved in contact-dependent T-cell activation of B-cells.

It can further be seen that the newly-submitted claims closely parallel claims recently issued to Lederman et al and assigned to Columbia University in U.S. Patent 5,993,816, on November 30, 1999. A copy of this patent is attached hereto for the convenience of the Examiner.

These claims should be allowable to Applicant for substantially the same reason that closely similar claims were allowed to Lederman et al. Also, the Examiner is respectfully advised that Lederman et al should not be applied as prior art under §102(e) because the effective filing date of this application is February 14, 1992, which is less than three months after November 15, 1991, the effective filing date of the Lederman '816

patent. Pursuant to §1.608, the undersigned respectfully asserts that there is a reasonable basis upon which the subject application should be entitled to an Interference judgment relative to the Lederman patent. Accordingly, a §131 Declaration is necessary.

Based thereon, Applicant hereby requests than an Interference be declared between this application and the Lederman '816 patent. For the convenience of the Examiner, the information required by §§1.607 and 1.608 is set forth under headings which correspond to the specific sections of §1.607 and §1.608.

(1) Identification of the Patent

Applicant seeks to provoke an interference between this application, having an effective filing date of February 14, 1992, and the Lederman patent, U.S. Patent No. 5,993,816, issued on November 30, 1999, having an effective filing date of November 15, 1991.

The claims of the Lederman patent are directed to use of a monoclonal antibodies which specifically bind to the antigen to which a particular monoclonal antibody, 5c8, specifically binds, and labeled forms thereof, to inhibit humoral immunity, immunoglobulin production, and B-cell activation, *in vitro* and *in vivo*.

(2) Suggestion of Proposed Count

Applicant hereby proposes the following Count to define the interfering subject matter. The proposed Count is an alternative Count prepared after careful consideration of the subject matter claimed by the respective parties.

An alternative Count is proposed because the present application and the Lederman patent define the same invention in different ways. More particularly, as described below, the patentable invention of the Count relates to use of monoclonal antibody which specifically bind an antigen selectively expressed on activated (not resting) T cells, which is involved in B cell activation, to inhibit humoral immunity immunoglobulin protection and B cell activation.

Specifically, in the Lederman patent this antigen is referred to by various names, i.e., "T-B cell activating molecule", "T-BAM", "CD40 ligand" (see column 2, lines 17-20) and the "5c8 antigen" based on its reactivity with a monoclonal antibody produced by a specific deposited hybridoma cell disclosed in the patent.

For example, at Col. 2, lines 17-20, the Lederman patent states that their

> "invention provides a monoclonal antibody which specifically recognizes and forms a complex with T-B cell activating molecule (T-BAM) (also know (SIC) as CD40 ligand) a protein located on the surface of activated T cells and thereby inhibits T cell activation of B cells."

The subject application similarly claims use of a monoclonal antibody which reacts with the same T cell antigen as the 5c8 monoclonal antibody of Lederman. However, in the subject application this same antigen is referred to by different names. Specifically, in the subject application, this antigen is referred to alternatively as the "CD40 counter receptor", "CD40CR", or is defined based on its reactivity with a specific monoclonal antibody produced by a deposited cell line, "MR1".

It is further noted that the 5c8 monoclonal antibody in the Lederman patent and the MR1 antibody of the subject application respectively specifically bind the human and murine counterparts of the same antigen expressed on activated T cells, which antigen is the counter receptor for CD40 expressed by B cells.

The fact that the MR1 antibody of the subject application binds the same antigen as the 5c8 antibody was conceded by the Patentees during prosecution in earlier Lederman patent 5,474,771 were involved in Interference. For example, the Patentees asserted at page 6 of their May 23, 1994 Response, the following:

> "MR1 is a hamster anti-T-BAM antibody that is similar with respect to mAb 5c8 with respect to its ability to inhibit contact dependent activation of B cells in vitro"...[i]t is therefore anticipated that both 5c8 and MR1 would have similar biological activities in humans and mice respectively".

Moreover, the Patentees stated "an antibody raised against a non-human T-BAM, such as MR1 which recognizes mouse T-BAM, is the best available animal model and would be accepted in the art".

The Patentees further stated at page 7 of this same Reply the following:

> "In a murine model of human autoimmune disease, anti-murine - T-BAM mAb MR1 was shown to inhibit collagen-induced antibodies."

Further at page 8, lines 8-9, the Patentees referred to the "therapeutic utility of an analogous anti-T-BAM mAb."

Thus, based on the Patentees' own admissions, it is clear that the subject application and the Lederman patent are both directed to use of monoclonal antibodies which bind the same T cell antigen to inhibit humoral immunity, immunoglobulin production, or B-cell activation. Similar to the parent application, which is involved in an earlier Interference with another Lederman patent (5,474,771) Applicant notes that the proposed Count has been drafted so as to encompass methods of using of monoclonal antibodies which bind either the murine or human counterpart of this T cell antigen, as these monoclonal antibodies, based on Patentee's own admissions, would be expected to possess "analogous" function and be obvious over one another.

The proposed Count is as follows:

> A method for inhibiting a humoral immune response, immunoglobulin production, and/or B-cell activation by contacting T-cells with an antibody that specifically binds to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916; or
>
> A method for inhibiting a humoral immune response, immunoglobulin production, and/or B-cell activation by contacting T-cells with an antibody that specifically binds to the protein specifically recognized by monoclonal antibody MR1 produced by the hybridoma having ATCC Accession Number HB 11048; or
>
> A method for inhibiting a humoral immune response, immunoglobulin production, and/or B-cell activation by contacting T-cells with an antibody that specifically binds to CD40CR.

(3) Identification of Patented Claims Corresponding to the Proposed Count

Claims 1-14 of the Lederman patent correspond to the proposed Count. These claims read as follows:

1. A method of inhibiting a humoral immune response, comprising contacting T cells with an antibody that binds specifically to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916.

2. A method of inhibiting immunoglobulin production, comprising contacting T cells with an antibody that specifically binds to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916.

3. A method of inhibiting activation of B cells, comprising contacting T cells with an antibody that specifically binds to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916.

4. A method of inhibiting a humoral immune response in an animal comprising the step of administering to the animal, in an amount effective to inhibit the humoral immune response, an antibody that binds specifically to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916.

5. A method of inhibiting immunoglobulin production in an animal, comprising the step of administering to the animal, in an amount effective to inhibit the immunoglobulin production, an antibody that binds specifically to a protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916.

6. A method of inhibiting activation of B cells in an animal, comprising the step of administering to the animal, in an amount effective to inhibit activation of B cells, an antibody that binds specifically to a

protein specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession Number HB 10916.

7. The method of claims 1, 2, 3, 4, 5, or 6, wherein the antibody is selected from the group consisting of: monoclonal antibodies, chimeric antibodies, human antibodies and humanized antibodies.

8. The method of claim 7, wherein the antibody 5c8 is produced by the hybridoma having ATCC Accession Number HB 10916.

9. The method of claim 7, wherein the antibody is conjugated to a therapeutic agent.

10. The method of claim 9, wherein the therapeutic agent is selected from the group consisting of: radioisotopes, toxins, toxoids and chemotherapeutic agents.

11. The method of claim 3 or 6, wherein the B cells are selected from the group consisting of: resting B cells and primed B cells.

12. The method of claim 4, 5 or 6, wherein the antibody is a chimeric monoclonal antibody, a humanized monoclonal antibody, a murine monoclonal antibody or a human monoclonal antibody.

13. The method of claim 4, 5 or 6, wherein the animal is a mammal.

14. The method of claim 13, wherein the mammal is a human.

It should be noted that Applicant is not conceding the validity of Claims 1-14, but are merely noting that they contain subject matter corresponding to the proposed Count. Essentially, all of the patent claims are directed to methods of using antibodies having the same binding specificity as the 5c8 antibody for inhibiting humoral immunity, immunoglobulin production, or B cell activation which, based on Patentees' own

admissions, bind the same antigen as MR1 (human counterpart) and would be expected to comprise analogous function. Applicant further notes that in accordance with 37 C.F.R. §1.606, the proposed Count corresponds to the broadest claims of the Lederman patent.

In particular, as discussed above, Claims 1-6 of the Lederman patent correspond identically to the first alternative of the proposed Count.

Dependent claims 7-14 similarly are directed to the same patentable invention as the Count. Claim 7 merely provides that the anti-5c8 antibody is a monoclonal, chimeric, human or humanized antibody which would have been obvious over the Count as these were well known types of antibodies at the time of the Lederman invention.

Claims 8 and 12 are directed to use of the monoclonal antibody produced by the deposited cell line HB 10916, which should be held unpatentable over the Count absent any unexpected results relative to the genus.

Claims 9 and 10 provide that the monoclonal antibody is conjugated to a therapeutic agent which should be held unpatentable over the Count since conjugation of effector (therapeutic) moieties to antibodies was well known as of the effective filing date of the Columbia patent.

Claim 11 provides that the administered antibody inhibits resting or primed B cells which should be held unpatentable over the Count as this is obvious over the Count which provides that the antibody inhibits B cell activation.

Claims 13 and 14 are unpatentable over the Count as they merely provide that humoral immunity, immunoglobulin production, or B cell activation is effected in a mammal or human, which would be obvious over the Count, based on the fact that *in vivo* suppression of humoral immunity, B cell activation, and immunoglobulin production, e.g., for treating allergies, and other antibody-related diseases, in mammals, and especially humans, was well known as of the effective filing date of the Columbia patent.

Thus, based on the foregoing, all of the claims of the Lederman patent correspond to the proposed Count.

(4) Requirements of 35 U.S.C. § 135(b) are Satisfied

The subject application and claims are being submitted less than one year after the issue date of the Lederman patent. Thus, the requirements of 35 U.S.C. §135(b) are satisfied.

Also, it is respectfully requested that this application be accorded special status as required under 37 C.F.R. §1.607(6)(b), because of the present Request to provoke an interference with an issued patent.

Further, according to §1.608(6)(d), Applicant understands that the Patentees will be given notice of the present Request to provoke an interference.

(5) *Prima Facie* Showing Required to Provoke an Interference between an Application and a Patent

The effective filing date of this application is February 14, 1992, which is less than three months after November 15, 1991, which is the effective filing date of the Lederman patent. The undersigned hereby asserts that there is a reasonable basis upon which the subject application should be entitled to a judgment relative to the Patentees.

(6) Identification of Claims in the Subject Application Corresponding to the Proposed Count

All of Claims 42-58 correspond to the proposed Count. In particular, all of these claims corresponds to the second or third alternative of the proposed Count. As required by 37 CFR §1.607(5)(ii), because these claims are newly-submitted, the basis for these claims in the as-filed application is set forth above.

As in the Lederman patent, Applicant's claims are directed to methods of using an antibody wherein said monoclonal antibody specifically binds an antigen expressed on activated T cells, and further wherein said antigen is the same antigen specifically bound by the MR1 antibody (which antigen is also referred to in the subject application as "CD40CR"), to inhibit humoral immunity, immunoglobulin production, or B-cell activation.